IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SAN ROCCO THERAPEUTICS, LLC,

Plaintiff,

v.

BLUEBIRD BIO, INC. and THIRD ROCK VENTURES, LLC,

Defendants.

Civil Action No. 21-1478-RGA

MEMORANDUM OPINION

Anne Shea Gaza, Samantha G. Wilson, YOUNG, CONAWAY, STARGATT & TAYLOR LLP, Wilmington, DE; Wanda D. French-Brown, Howard S. Suh, James H. McConnell (argued), Mary Jean Kim, FOX ROTHSCHILD LLP, New York, NY; Joe G. Chen, FOX ROTHSCHILD LLP, Lawrenceville, NJ,

Attorneys for Plaintiff.

Jack B. Blumenfeld, Jeremy A. Tigan, MORRIS, NICHOLS, ARSHT & TUNNELL LLP, Wilmington, DE; Eric W. Dittman (argued), Joshua M. Bennett, Max H. Yusem, Krystina L. Ho (argued), PAUL HASTINGS LLP, New York, NY; Naveen Modi, PAUL HASTINGS LLP, Washington, D.C.,

Attorneys for Defendants.

May 29, 2024

ANDREWS, U.S. DISTRICT JUDGE:

Before me is the issue of claim construction of multiple terms in U.S. Patent No. 7,541,179 ("the '179 patent") and U.S. Patent No. 8,058,061 ("the '061 patent"). The parties submitted a Joint Claim Construction Brief. (D.I. 141). At my request, the parties submitted supplemental letter briefing on the basic and novel properties of the patented invention. (D.I. 151, 152). I heard oral argument on March 20, 2024. (Markman Tr.).[1]

I. BACKGROUND

On October 21, 2021, Plaintiff San Rocco Therapeutics filed a complaint against Defendants Bluebird Bio and Third Rock Ventures, alleging infringement of the '179 and '061 patents. (D.I. 1). While Plaintiff has since amended its complaint twice, both patents remain asserted in this action. (*See* D.I. 39). The asserted patents are directed towards vectors useful for the treatment of hemoglobinopathies. ('179 patent, Abstract; '061 patent, Abstract). The patents are related; the '061 patent is a divisional of the '179 patent. ('061 patent, 1:8–13). The asserted patents claim a priority date of June 29, 2001. (*Id.*; '179 patent, 1:7–11).

II. LEGAL STANDARD

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (internal quotation marks omitted). "'[T]here is no magic formula or catechism for conducting claim construction.' Instead, the court is free to attach the appropriate weight to appropriate sources 'in light of the statutes and policies that inform patent law.'" *SoftView LLC v. Apple Inc.*, 2013 WL 4758195, at *1 (D. Del. Sept. 4, 2013) (alteration in

[1] Citations to the transcript of the argument, which is not yet docketed, are in the format "Markman Tr. at __."

original) (quoting *Phillips*, 415 F.3d at 1324). When construing patent claims, a court considers the literal language of the claim, the patent specification, and the prosecution history. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977–80 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). Of these sources, "the specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (internal quotation marks omitted). "While claim terms are understood in light of the specification, a claim construction must not import limitations from the specification into the claims." *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349, 1354 (Fed. Cir. 2012) (citing *Phillips*, 415 F.3d at 1323).

"[T]he words of a claim are generally given their ordinary and customary meaning. . . . [Which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* at 1312–13 (citations and internal quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to [an] ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). "In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

When a court relies solely upon the intrinsic evidence—the patent claims, the specification, and the prosecution history—the court's construction is a determination of law. *See Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 331 (2015). The court may also make factual findings based upon consideration of extrinsic evidence, which "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony,

dictionaries, and learned treatises." *Phillips*, 415 F.3d at 1317–19 (quoting *Markman*, 52 F.3d at 980). Extrinsic evidence may assist the court in understanding the underlying technology, the meaning of terms to one skilled in the art, and how the invention works. *Id.* Extrinsic evidence, however, is less reliable and less useful in claim construction than the patent and its prosecution history. *Id.*

III. CONSTRUCTION OF AGREED-UPON TERMS

I adopt the following agreed-upon constructions:

Claim Term	Claims	Construction
"LCR"	'179 patent, claims 1, 10, 19, 22–24 '061 patent, claims 1–3, 5–8, 11–12, 15	"locus control region"
"HS"	'179 patent, claims 1, 10, 19, 22–24 '061 patent, claims 1–3, 5–8, 11–12, 15	"hypersensitive site"
"contiguous"	'179 patent, claims 1, 10, 19, 22 '061 patent, claims 1–3, 5–8, 11–12, 15	"1. touching; in contact, or 2. In close proximity without actually touching; near."

IV. CONSTRUCTION OF DISPUTED TERMS

The parties agree that claim 1 of the '179 patent and claim 1 of the '061 patent are representative for the purpose of claim construction. Those claims state:

> 1. A recombinant vector comprising a nucleic acid encoding a ***functional globin*** operably linked to a 3.2-kb nucleotide fragment which ***consists essentially of*** three contiguous nucleotide fragments obtainable from a human β-globin locus control region (LCR), the three fragments being ***a BstXI and SnaBI HS2-spanning nucleotide fragment*** of said LCR, ***a BamHI and HindIII HS3-spanning nucleotide fragment*** of said LCR and ***a BamHI and BanII HS4-spanning nucleotide fragment*** of said LCR, said vector providing expression of the globin in a mammal in vivo.

('179 patent, 11:55–65 (disputed terms bolded and italicized)).

> 1. An isolated mammalian hematopoietic progenitor cell or an isolated mammalian stem cell comprising a recombinant lentiviral vector which comprises a nucleic acid encoding a ***functional globin*** operably linked to a 3.2-kb nucleotide fragment which ***consists essentially of*** three contiguous nucleotide fragments obtainable from a human β-globin locus control region (LCR), the three fragments being ***a BstXI and SnaBI, HS2-spanning nucleotide fragment*** of said LCR, ***a BamHI and HindIII, HS3-spanning nucleotide fragment*** of said LCR and ***a BamHI and BanII, HS4-spanning nucleotide fragment*** of said LCR, said vector providing expression of the globin in a mammal in vivo.

('179 patent, 11:55–65 (disputed terms bolded and italicized)).

1. **"consists essentially of" ('179 patent, claims 1, 10, 19, 22–24; '061 patent, claims 1–3, 5–8, 11–12, 15)**

    a. *Plaintiff's proposed construction*: "necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention"
    b. *Defendants' proposed construction*: "necessarily includes the specific assembly of three recited LCR fragments, which is specifically defined by (1) the HS spanned by each fragment, (2) the restriction sites defining the ends of each fragment, (3) the size of each fragment, and importantly (4) the overall combined size of the three fragments to provide a single nucleotide fragment of 3.2 kb, and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention, but the combined size of the three HS-spanning fragments so closely approximates 3.2kb that the number of additional nucleotides that could be added to (or removed from) this fragment is relatively few and nonmaterial"
    c. *Court's construction*: "necessarily includes the specific assembly of three recited LCR fragments, which is specifically defined by (1) the HS spanned by each fragment, (2) the restriction sites defining the ends of each fragment, (3) the size of each fragment, and (4) the overall combined size of the three fragments to provide a single nucleotide fragment of 3.2 kb, and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention, but the combined size of the three HS-spanning fragments so closely approximates 3.2kb that the number of additional nucleotides that could be added to (or removed from) this fragment is relatively few and nonmaterial"

"While 'consisting essentially of' usually 'signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention,' . . . a patentee can alter that typical meaning." *Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335, 1343–44 (Fed. Cir. 2008) (citing *PPG Indus. v. Guardian*

Indus. Corp., 156 F.3d 1351, 1354 (Fed. Cir. 1998)). A court should not give a claim term its ordinary meaning "if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002).

Plaintiff maintains that I should adopt the usual definition of "consists essentially of." Defendants contend that I should apply the definition that the Patent Applicants established during patent prosecution. (*See* D.I. 142-1, Ex. E-22, at JA0379–80). Plaintiff's counsel conceded that Defendants' construction was, at least earlier in the patent application process, the interpretation adopted by the Applicants. (Markman Tr. at 11:3–12:7). Plaintiff nevertheless maintains that this construction does not capture the claim language as issued. (*Id.* at 11:3–14). In an Examiner's Amendment shortly before allowance, the relevant portion of the claim language was modified to recite:

> . . . the three fragments being [[an]] a BsxtXI and SnaBI HS2-spanning nucleotide fragment of said LCR ~~extending between BstXI and SnaBI restriction sites of a human B-globin locus control region (LCR)~~, [[an]] a BamHI and HindIII HS3-spanning nucleotide fragment ~~extending between BamHI and HindIII restriction sites~~ of said LCR and [[an]] a BamHI and BanII HS4-spanning nucleotide fragment ~~extending between BamHI and BanII restriction sites~~ of said LCR . . . .

(D.I. 142-1, Ex. E-23, at JA0404–05). Plaintiff argues that Defendants' construction no longer accurately represents the claim scope due to the deletion of the phrase "extending between." (D.I. 141 at 27).

As an initial matter, I disagree with Plaintiff's claim that Defendants' construction relies on disclaimer. (*See id.* at 16; Markman Tr. at 13:17–22). Defendants derive their construction based on language the Applicants used during patent prosecution. (*See* D.I. 141 at 21; Markman Tr. at 28:11–31:13; *see also* D.I. 142-1, Ex. E-22, at JA0377–78). Defendants' position is based on lexicography.

Plaintiff relies on a line of cases that generally stands for the principle that "claim construction cannot be used to reintroduce deleted matter back into the claims." (D.I. 141 at 17 (citing *Blackbird Tech LLC v. ELB Elecs., Inc.*, 895 F.3d 1374, 1379 (Fed. Cir. 2018); *Laryngeal Mask Co. v. Ambu*, 618 F. 3d 1367, 1372-73 (Fed. Cir. 2010))). Plaintiff's position, however, relies on an understanding that the edits removing "extending between" impacted claim scope. Not all modifications to claim language represent substantive additions or deletions of claim elements; some changes are simply rewordings of the claim language to more accurately capture existing claim limitations.

To determine whether amendments alter the claim scope, "[w]e look at what an ordinarily skilled artisan would understand about claim scope from reading the prosecution history."[2] *Blackbird*, 895 F.3d at 1378 (emphasis omitted). In *Blackbird*, the patent applicant "expressly eliminated from the claim a fastening mechanism that secures the attachment surface to the ballast cover and replaced it with a fastening mechanism that secures the attachment surface to the illumination surface." *Id.* The applicant agreed to make these amendments, following an interview with the examiner, "to resolve 112 issues." *Id.* The defendants argued that "the prosecution history is ambiguous because the examiner's requirement that the change be made to resolve § 112 issues provides no explanation for the amendment." *Id.* (cleaned up). The Federal Circuit rejected this argument, noting, "Any skilled artisan would understand that if an examiner requires an amendment for § 112 reasons it is an amendment required for patentability." *Id.* Based on its review of the prosecution history, the court concluded that "no skilled artisan would

[2] Plaintiff appears to argue that prosecution history from before the "extending between" amendment is irrelevant to construing the final claim language. (D.I. 141 at 27). Even if the significance of earlier prosecution history might be tempered by context, the cited case law does not support ignoring such evidence altogether.

understand this claim to require a fastening mechanism connecting the ballast cover to the attachment surface when that very limitation was expressly removed from the claim to secure patentability with the examiner's blessing and agreement." *Id.*

In the present action, a "review [of] the prosecution history from the perspective of an ordinary artisan" demonstrates that deletion of the "extending between" phrase was directed towards form and did not alter the scope of the claims.

In a Final Office Action issued on June 3, 2008, the Patent Examiner "objected" to the Applicants' proposed claim language, for what would become claim 1 of the '179 patent, based on certain "informalities." (D.I. 142-1, Ex. E-21, at JA0360). The Examiner proposed the following changes to the claim language:

> . . . which consists essentially of an HS-2 spanning ~~nucleotide fragment extending between~~ BstXI and SnaB1 restriction ~~sites of~~ fragment from a human β-globin locus control region (LCR), an HS3-spanning ~~nucleotide fragment extending between~~ BanHI and HindIII restriction ~~sites of~~ fragment from said LCR and an HS-4 spanning ~~nucleotide fragment extending between~~ BamHI and BanII restriction ~~sites of~~ fragment from said LCR.

(*Id.*) (Applicants' language and Examiner's language combined and emphasis added to convey recommended additions and deletions). Though the Examiner's proposal does not match the final issued claim language verbatim, it also suggests removal of "extending between." As Defendants' counsel noted, "objections" made by an examiner go to the form of a claim; in contrast, "rejections" are directed to the claim's substance. (Markman Tr. at 35:16–3; *accord* MPEP § 706.01). It follows that the examiner understood the deletion of "extending between" to not impact claim scope.

Plaintiff contends that the Applicants rejected the examiner's proposed wording and explained why it was important to maintain the "extending between" phrase. (D.I. 141 at 28). While the Applicants did object to the Examiner's proposal in the December 3, 2008

Amendment and Response After Final Action, their response focused on the change from "nucleotide fragment" to "restriction sites" and did not directly raise any issues, substantive or otherwise, with the removal of "extending between" in particular. (*See* D.I. 142-1, Ex. E-22, at JA0377–78 ("As Applicants understand this objection, the Examiner recommends that the elements be recited as particular HS-spanning restriction fragments. Applicants believe that characterization of these elements as nucleotide fragments more accurately reflects the nature of these elements.")). Applicants' response makes clear that their objection was directed towards which "language [was] preferable." (*See id.* at JA0378 (focusing on "ensur[ing] that there is no ambiguity"); *id* ("All of these forms may colloquially be referred to as restriction fragments but are more fully described as a subset of nucleotide fragments that extend between particular restriction sites.")).

In the above-referenced Final Office Action, the Examiner also rejected the aforementioned claim as anticipated because "the specification does not define the use of the term 'consisting essentially of.'" (*Id.*, E-21, at JA0361–62). She advised the Applicants, "Absent a clear indication in the specification or claims as to what is considered a material change in the basic and novel characteristics of 'consisting essentially of,' it will be construed as equivalent to 'comprising.'" (*Id.* at JA0361–62 (citing MPEP § 2111.03)). The Applicants responded:

> According to the invention, the basic and novel properties of the claimed subject matter are achieved by the choice and combination of the three specific nucleotide fragments from a human β-globin LCR that produce a vector capable of expressing a functional globin *in vivo* when the vector is introduced into a mammal. The choice of the three nucleotide fragments recited in Claim 1 is specifically defined by (1) the HS spanned by each fragment, (2) the restriction sites defining the ends of each fragment, (3) the size of each fragment, and importantly, (4) the overall combined size of the three fragments to provide a single nucleotide fragment of 3.2 kb.
>
> . . . .

> [T]he combined size of the three HS-spanning fragments so closely approximates 3.2kb, that the number of additional nucleotides that could be added to (or removed from) this fragment is relatively few and nonmaterial.

(D.I. 142-1, Ex. E-22, at JA0379–80). This language serves as the foundation for Defendants' proposed definitions for "consisting essentially of" and the basic and novel properties of the invention. (*See* D.I. 141 at 17; D.I. 151 at 1). It is also consistent with the importance Plaintiff's IPR briefing attributes to the "correct size" of the LCR fragments. (D.I. 143-1, Ex. H-4, JA0888 ("[T]he true breakthrough of the invention was . . . in developing a groundbreaking expression vector system that employed the correct size of LCR hypersensitive regions—not too big and not too small . . . .")). In contrast, Plaintiff's suggested definition for the basic and novel properties of the invention is a "3.2-kb upper limit of Locus Control Region ('LCR') material (a type of genetic material found in human DNA)." (D.I. 152 at 1 of 3). At oral argument, Plaintiff argued the fragments were also subject to a lower size limit of 1 kb.[3] (Markman Tr. at 57:3–7). Plaintiff's suggested range, from 1 to 3.2 kb, conflicts with Plaintiff's IPR position that the patented invention's novel contribution was its "'Goldilocks' approach in determining the right size of LCR fragments." (D.I. 143-1, Ex. H-4, JA0888).

Following the Final Office Action and the Applicants' response, the Examiner and Applicants had a telephone interview on January 8, 2009. (D.I. 142-1, Ex. E-23, at JA0404). An Examiner's Amendment, which contained the final version of the claim language, was then issued on January 26, 2009. (*Id.* at JA404–05). Plaintiff's argument focuses on the fact that no record exists of what was discussed during the interview. (Markman Tr. at 12:5–13:16). The

[3] It is not clear how Plaintiff derived this lower limit. At oral argument, Plaintiff's counsel stated that the fragment "does need to be more than the core element" based on "the prior art situation," the specification, and what is "known to POSITAs." (Markman Tr. at 56:21–58:6). This explanation provides little insight as to how Plaintiff arrived at its proposed lower limit.

lack of evidence about the contents of the discussion at the interview does not render earlier prosecution history irrelevant. *See Blackbird*, 895 F.3d at 1378 ("A person of ordinary skill in the art may not be able to divine what transpired between the Applicants and the examiner in that interview that caused the change in claim language and scope. That is irrelevant to the issue. We look at what an ordinarily skilled artisan would understand about claim scope from reading the prosecution history." (emphasis omitted)). Nor does the lack of evidence support Plaintiff's position that the Examiner and the Applicants flip-flopped from their original understanding that deletion of the "extending between" language was directed to form, not substance. The prosecution history, as a whole, demonstrates that the "extending between" language removal does not affect claim scope.

Plaintiff notes that Defendants' construction requires both specified fragments, which add up to 3.232 kb in size, and that the vector remain "open to unlisted ingredients." (D.I. 141 at 19–20). It argues that, under Defendants' construction, there is no room for any unlisted ingredients because the specified fragments already add up to the 3.2 kb size requirement in the claim language. As the Applicants explained, however, "any additional nucleotides added to the 3.2 kb fragment that cause the fragment to exceed 3.2 kb, would alter a basic and novel property of the invention." (D.I. 142-1, Ex. E-22, JA0380). As a result, "the number of additional nucleotides that could be added to (or removed from) [the 3.2 kb] fragment is relatively few and non-material." The prosecution history establishes that Defendants' construction does leave room for "unlisted ingredients" by specifying that only negligible additions can be introduced.

For the foregoing reasons, I find Defendants' construction to be an accurate interpretation of the definition of "consists essentially of" adopted by the Applicants. Defendants' construction

does contain a term, "importantly," that I find superfluous. (*See* Markman Tr. at 31:14–23). Aside from deletion of this term, I otherwise adopt Defendants' construction.

2. **"a BstXI and SnaBI HS2-spanning nucleotide fragment" / "a BstXI and SnaBI, HS2-spanning nucleotide fragment" ('179 patent, claims 1, 10, 19, 22–24; '061 patent, claims 1–3, 5–8, 11–12, 15)**

    a. *Plaintiff's proposed construction*: "a nucleotide fragment found within the BstXI and SnaBI HS2 region"
    b. *Defendants' proposed construction*: "a fragment that is located at nucleotides 8055-8911 and has a size of 857 bp"
    c. *Court's construction*: "a fragment that is located at nucleotides 8055-8911 and has a size of 857 bp"

3. **"a BamHI and HindIII HS3-spanning nucleotide fragment" / "a BamHI and HindIII, HS3-spanning nucleotide fragment" ('179 patent, claims 1, 10, 19, 22–24; '061 patent, claims 1–3, 5–8, 11–12, 15)**

    a. *Plaintiff's proposed construction*: "a nucleotide fragment found within the BamHI and HindIII HS3 region"
    b. *Defendants' proposed construction*: "a fragment that is located at nucleotides 3878-5172 and has a size of 1295 bp"
    c. *Court's construction*: "a fragment that is located at nucleotides 3878-5172 and has a size of 1295 bp"

4. **"a BamHI and BanII HS4-spanning nucleotide fragment" / "a BamHI and BanII, HS4-spanning nucleotide fragment" ('179 patent, claims 1, 10, 19, 22–24; '061 patent, claims 1–3, 5–8, 11–12, 15)**

    a. *Plaintiff's proposed construction*: "a nucleotide fragment found within the BamHI and BanII, HS4 region"
    b. *Defendants' proposed construction*: "a fragment that is located at nucleotides 308-1388 and has a size of 1080 bp"
    c. *Court's construction*: "a fragment that is located at nucleotides 308-1388 and has a size of 1081 bp"

The parties' dispute over terms 2, 3, and 4 stems from the same issue discussed with regard to term 1—the effect of deleting the phrase "extending between" from the claim language. (*See* Markman Tr. at 4:9–16). Plaintiff's construction relies on its understanding that the "extending between" deletion impacted claim scope. (D.I. 141 at 32). Defendants' construction requires a specified size and location for each fragment and is derived from the prosecution

history and prior versions of the claim language. (*Id.* at 36–37 (citing D.I. 142-1, Ex. E-7, at JA0155; *id.*, E-16, at JA0249, JA0261–62; *id.*, E-17, at JA0276–77)). At oral argument, Plaintiff's counsel conceded that Defendants' constructions would be correct if not for the deletion of "extending between."[4] (Markman Tr. at 49:11–51:18). As I find the removal of "extending between" does not alter claim scope, I adopt Defendants' constructions. I nevertheless address Plaintiff's remaining arguments related to terms 2, 3, and 4.

Plaintiff argues its proposed constructions are consistent with the use of the term "spanning" in the intrinsic record. (D.I. 141 at 32). Plaintiff points to an article, submitted during prosecution of the provisional application, that refers to both "small elements spanning DNAs HS2, HS3 and HS4" and "large elements spanning HS2, HS3 and HS4." (*Id.* at 32–33 (citing D.I. 142-1, Ex. C, JA0036)). Plaintiff maintains, "If spanning referred to the entire region, there could be no small versus large elements spanning the same region." (*Id.* at 33). The Applicants' reliance on the article for its use of "spanning" is doubtful given the absence of any discussion of the subject during prosecution. (*See* D.I. 142-1, Ex. C, at JA0034–35). Moreover, Plaintiff has not convinced me that Defendants' reading of the article—that "small elements" and "large elements" are discussed as references to specific fragments (with specified sizes and restriction sites) identified in other articles—is incorrect. (*See* D.I. 141 at 39–40). As I stated at oral argument, it seems strange to argue "spanning" does not refer to extending between

[4] Plaintiff's counsel did suggest that I "tweak [Defendants' construction] slightly" to indicate the fragment endpoints were ranges of numbers rather than one specific number. (*See* Markman Tr. at 50:1–8 ("[T]he restriction site location . . . is not a individual-specific number. It's actually a range of numbers . . . . It's corresponding to, say, 10 to 14, rather than, you know, the number 11.")). Plaintiff's concern appears to be a non-issue as the adopted definition for "consists essentially of" allows for the addition or removal of "relatively few and nonmaterial" nucleotides. I also believe Defendants' construction comports with the Applicants' discussion of specific fragment sizes and endpoint locations in the prosecution history. (*See* D.I. 142-1, E-14, at JA0230–35; *id.*, E-17, at JA0275–77 ¶¶ 35–46; *id.*, Ex. E-22, at JA0379–80; D.I. 151 at 1).

two endpoints. (Markman Tr. at 52:14–57:18; *see Span*, MERRIAM-WEBSTER, https://www.merriam-webster.com/dictionary/span (providing, as one definition, "to extend across")).

Plaintiff and Defendants dispute the impact of a portion of the specification on the Applicants' definition of "spanning":

> "In accordance with the invention, a recombinant lentiviral vector is provided comprising:
> . . . .
> (b) large portions of the β-globin locus control regions which include large portions of DNase I hypersensitive sites HS2, HS3 and HS4. The regions may be the complete site or some lesser site which provides the same functionality as the specific sequences set forth below.

('179 patent, 1:48–55). Plaintiff argues the statement that "regions may be the complete site or some lesser site" makes clear that "spanning" fragments need not extend across entire regions. (D.I.141 at 33). Defendants argue the surrounding context in the specification indicates this sentence is describing a disclaimed claim element. (D.I. 141 at 40 –42). The "large portions of the β-globin locus control regions which include large portions of DNase I hypersensitive sites HS2, HS3 and HS4" language matches, verbatim, an earlier version of claim language rejected by the Examiner. (*See* D.I. 142-1, Ex. E-6, at JA0136–45; *id.*, Ex. E-5 at JA0113). The Examiner opposed this claim language for attempting to claim "any recombinant vector expressing a functional β-globin gene and such a 'large portion of the β-globin locus control region.'" (*Id.*, Ex. E-6, at JA0137). Applicant then amended the claims to remove the term "large" and to include specific sizes for each fragment. (*See id.*, Ex. E-7, at JA0155; *see also id.* at JA0161). While Plaintiff maintains that specification does not treat "large portions" and "regions" as the same thing (D.I. 141 at 47), Defendants' interpretation is certainly plausible based on the surrounding context.

The article and the disputed portion of the specification are, at best, ambiguous about the meaning of "spanning." Parts of the prosecution history, however, tie the "spanning" fragments to specific locations and sizes. (*See id.*, Ex. E-16, at JA0262 ("[T]he HS2-spanning fragment . . . is located at nucleotides 8055-8911 and has a size of 857 bp; the HS4-spanning fragment . . . is located at nucleotides 308-1388 and has a size of 1080 bp and the HS3-spanning fragment . . . is located at nucleotides 3878-5172 and has a size of 1295 bp.")). Defendants' construction appears consistent with usage of "spanning" in the intrinsic record.

Plaintiff argues that Defendants' construction of term 2 "contradicts" a dependent claim. (D.I. 141 at 34). Claim 24 of the '179 patent, which depends on independent claim 23 of the same patent ('179 patent, 14:28), covers a vector that includes a HS-2 spanning fragment with a size of 840 bp. (*Id.* 3:24–25, 4:9–11). Under Defendants' construction, claim 23 covers a vector that includes a HS-2 spanning fragment with a size of 857. (*See id.*, 14:14–27). Based on the larger size of the claim 23 fragment, Plaintiff argues that Defendants' definition results in claim 23 excluding the embodiment claimed in claim 24. (D.I. 141 at 34). As explained, Defendants' proposed construction for "consists essentially of" allows additional nucleotides to be "added to (or removed from) [the claimed] fragment" provided they are "relatively few and nonmaterial." As a result, this size discrepancy does not present an "inconsistency" between independent and dependent claims under Defendants' construction. (D.I. 141 at 28).

For the reasons stated above, I adopt Defendants' constructions for terms 2 and 3. Apart from rectifying the incorrectly calculated fragment size, I also adopt Defendants' construction for term 4. (*See* Markman Tr. at 9:18–10:12).

5. "functional globin" ('179 patent, claims 1, 10, 19, 22–24; '061 patent, claims 1–3, 5–8, 11–12, 15)

a. *Plaintiff's proposed construction*: "a globin, such as β-globin, or γ-globin, which is effective to provide therapeutic benefits for treatment of hemoglobinopathies, including β-thalassemia and sickle-cell disease"
b. *Defendants' proposed construction*: "a globin that does not produce a hemoglobinopathy phenotype, and which is effective to provide therapeutic benefits to an individual with a defective globin gene"
c. *Court's construction*: "a globin that does not produce a hemoglobinopathy phenotype, and which is effective to provide therapeutic benefits to an individual with a defective globin gene"

For the reasons explained at oral argument, I adopt Defendants' proposed construction for "functional globin." (*See id.* at 71:14–82:25, 83:22–90:13). It is clear that Plaintiff's objection to this construction stems from a concern over potential jury confusion rather than any substantive disagreement over the term's definition. (*See id.* at 85:4–89:13). I do not believe Plaintiff's concern is justified. I reserve the right to revisit the construction should jury confusion develop into an actual issue at a later stage of this case.

V. CONCLUSION

Within five days the parties shall submit a proposed order consistent with this Memorandum Opinion.